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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,821	02/25/2005	Joachim Kralik	MERCK-2978	9167

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EXAMINER	
CUTLIFF, YATE KAI RENE	
ART UNIT	**PAPER NUMBER**
1621	

MAIL DATE	DELIVERY MODE
12/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,821	KRALIK ET AL.	
	Examiner	Art Unit	
	Yate' K. Cutliff	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24 and 25* is/are allowed.

6)☒ Claim(s) *1-7,10-14,17 and 18* is/are rejected.

7)☒ Claim(s) *8,9,15,16 and 19-23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/25/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. Rejection of claims 1-3, 6, 7 and 10 – 14, under 102(b), in light of Applicant's amendment, is withdrawn.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 1 – 7, 10 – 14, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over anticipate by G. Helmchen et al. "HOUBEN-WEYL Methods of Organic Chemistry; Additional and Suppl. V01. to the 4th ED." Vol. [E 21 D, Stereoselecive Synthesis (Pages 3955-3956, Chapter 2.2.1.2.7) 30 November 1995 (1995-11-30), George Thieme Verlag, Stutgart - New York.

The rejected claims, inter alia, claim a process for enantioselective preparation of amino alcohols of formula I by enantioselective hydrogenation of amino ketones of

formula II, with R1 - R4, and n = 1, 2, or 3, in the presence of a non-racemic catalyst, characterized in that the catalyst is a transition metal complex in which the transition metal is complexed to a chiral diphosphine ligand A or ligand B. See the complete description in the previous office action.

Helmchen et al. discloses a process that involves the hydrogenation of alpha-amino ketones that results in the formulation of alpha-amino alcohols which are biologically important compounds e.g., adrenergic drugs. (see page 3995). The process of Helmchen is substantially identical to Applicant's process when n = 1, the non-racemic catalyst is $[Rh(COD)Cl]_2$/BPPFOH, and yields of 100%. See detailed description in 102(b) of previous Office Action.

Helmchen et al. fails to explicitly disclose the process where n=1, and the substitution of H or methyl on the ring structure of R1.

However, where n=1 this chemical change may be considered a first homologenation, replacing the methyl groups with the ethyl group. The case law on concerning prima facie obviousness of structurally similar compounds is well-established. Courts have held, "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a prima facie case of obviousness." *Dillon*, 919 F.2d at 692 [16 USPQ2d 1897]. Further, in order to find a prima facie case of unpatentability in such instances, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required. *Id.* (citing *In re Jones*, 958 F.2d 347 [21 USPQ2d

1941] (Fed. Cir. 1992); *Dillon*, 919 F.2d 688 [16 USPQ2d 1897] ; *Grabiak*, 769 F.2d 729 [226 USPQ 870]; *In re Lalu*, 747 F.2d 703 [223 USPQ 1257](Fed. Cir. 1984)). Furthermore, Failure of prior art to disclose or render obvious method for making any composition of matter, whether compound or mixture of compounds, precludes conclusion that composition would have been obvious. *In re Gross and Flanigen*, 592 F2d 1161 [201 USPQ 57, 58]

Helmchen et al. discloses a method for making amino alcohols of Applicant's formula I, using identical ketones and non-racemic catalyst.

Applicant's arguments with respect to claim 1 - 7 and 10 - 14 have been considered but are moot in view of the new ground(s) of rejection which were necessitated, by Applicant's amendment to claim 1 filed in the Response of November 6, 2007.

With regard to R3 and R4 being H or methyl as substituents of R1, it is well within the purview of an ordinary artesian to make these substitutions. Therefore, it would have been obvious at the time Applicant's invention was made to have H and methy as substituents on R1 to tweak the process

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the reference, it is apparent that a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common senses. In this instance the fact that a combination was

obvious to try might show that it was obvious under §103. KSR, 550 U.S. al, 82 USPQ2d at 1397.

Allowable Subject Matter

5. Claim 8 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, as it relates to the R1 = a heterocyclic as elected or carbocyclic, n = 2,3 and the transition-metal is a rhodium or salts thereof.

6. Claim 9 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, as it relates to the R1 = a heterocyclic as elected or carbocyclic and n = 2,3, and the transition metal is rhodium or salts thereof.

7. Claims 15, 16, 19 - 23 and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, as it relates to the R1 = heterocyclic as elected or carbocyclic, and the transition-metal is a rhodium or salts thereof.

8. The process of claims 24 and 25 are allowed.

9. The process of claims 24 and 25 are allowed because none of the references teach the process for preparing the amino alcohol from the enantioselective hydrogenation reaction of an amino ketone, where R1 is a heterocyclic with n= 1, 2 or 3; and using a transition-metal complex where the transition metal is complexed to ligand A as claimed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yate' K. Cutliff whose telephone number is (571) 272-9067. The examiner can normally be reached on M-TH 8:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272 - 0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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